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Receipt

PATENT  
ATTORNEY DOCKET NO. UCSD1140-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Robert K. Naviaux  
Application No.: 09/889,251  
Filed: November 1, 2001  
Title: METHODS OF TREATMENT OF MITOCHONDRIAL DISEASES

Commissioner for Patents  
Office of Initial Patent Examination  
Customer Service Center  
P.O. Box 1450  
Alexandria, VA 22313-1450

**TRANSMITTAL LETTER**

Sir:

Transmitted herewith for filing in connection with the above-identified patent application, please find the following:

- (1) Request for Corrected Filing Receipt; (2 pgs)
- (2) Copy of Filing Receipt reflecting changes; (1 pg)
- (3) Copy of 1st Page of Patent Application; (1 pg) and
- (4) Return postcard.

CERTIFICATION UNDER 37 CFR §1.8

I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, 8-24-04, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

*Yinix M. Naviaux*

(Name of Person mailing Paper)

*Yinix M. Naviaux* 8-24-04

Date

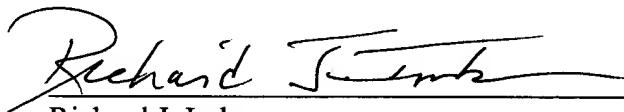
In re Application of:  
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PATENT  
Attorney Docket No.: UCSD1140-1

No fee is deemed necessary in connection with the filing of this paper. However, if any fee is required, the Commissioner is hereby authorized to charge the amount of this fee, or credit any overpayments, to Deposit Account No. 50-1355. A copy of this Transmittal Letter is enclosed.

Respectfully submitted,

Date: August 24 2004



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**USPTO CUSTOMER NO. 28213**

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**REQUEST FOR CORRECTION OF FILING RECEIPT**

Sir:

This Communication is submitted to request correction of the filing receipt in reference to the above-identified application. The data requiring correction is indicated in yellow highlight on the attached copy of the filing receipt and herein in **BOLD**.

Please correct the first word of the title from "**Method**" to **-METHODS-**.

Applicant accordingly requests the correction be made of record.

CERTIFICATION UNDER 37 CFR §1.8

I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, 8-24-04, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Yinna M. Najar  
(Name of Person mailing Paper)

Yinna M. Najar  
(Signature of Person Mailing Paper)

8-24-04  
Date

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APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	DRAWINGS	TOT CLAIMS	IND CLAIMS
09/889,251	11/01/2001	1614	506	UCSD1140-1		27	4

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CONFIRMATION NO. 9760  
 REPLACEMENT FILING RECEIPT



\*OC00000007403364\*

Date Mailed: 01/31/2002

Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Customer Service Center. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).

**Applicant(s)**

Robert K. Naviaux, San Diego, CA;

**Domestic Priority data as claimed by applicant**

THIS APPLICATION IS A 371 OF PCT/US00/04663 02/23/2000  
 WHICH CLAIMS BENEFIT OF 60/121,588 02/23/1999

**Foreign Applications****Projected Publication Date:** Not Applicable, filed prior to November 29,2000**Non-Publication Request:** No**Early Publication Request:** No**\*\* SMALL ENTITY \*\*****Title**

Method of treatment of mitochondrial disorders

**Preliminary Class**

add

514

## METHODS OF TREATMENT OF MITOCHONDRIAL DISORDERS

### FIELD OF THE INVENTION

The present invention relates generally to mitochondrial disorders, and more specifically to the treatment of mitochondrial disorders by the administration of a 5 pyrimidine-based nucleoside such as triacetyluridine.

### BACKGROUND OF THE INVENTION

Mitochondrial diseases occur as inherited, sporadic, and acquired forms. Inherited forms of mitochondrial disease have a high mortality and morbidity. The most severe forms, such as Leigh syndrome (subacute necrotizing 10 encephalomyopathy) have a mortality of up to 50% per year after diagnosis. Multifactorial forms of mitochondrial disease include much more common disorders such as Huntington's disease, Parkinson's disease, Alzheimer's disease, and even certain forms of diabetes, heart disease, migraine, and stroke. Indeed the process of aging itself has been linked to progressive declines in mitochondrial function. 15 Mitochondrial diseases are defined as disorders of mitochondrial metabolism that arise from a genetic defect in nuclear or mitochondrial DNA. These may be maternally inherited, inherited as conventional Mendelian disorders, or acquired as new somatic mutations. The disorders may be manifested at any genetic level, from DNA and RNA, to protein. They may affect mitochondrial DNA replication, 20 transcription, the transport of macromolecules into or out of mitochondria, or the function of macromolecules at their site of action within mitochondria. Historically, discussions of pathogenesis in mitochondrial disease have focused on the degradative (oxidative) functions of mitochondria. However, a number of the symptoms of mitochondrial disease may be related to essential biosynthetic (non-degradative) 25 functions of the organelles that are often overlooked. One biosynthetic function of mitochondria is the synthesis of uridine.

Patients with a variety of different mitochondrial disorders may be functionally deficient in uridine because the rate-limiting step in *de novo* pyrimidine synthesis (Dihydroorotate CoQ Oxidoreductase, EC 1.3.99.11) is located on the inner 30 membrane of mitochondria and coupled to the electron transport chain. Cells with